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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,377	07/27/2001	Alexander Olek	81702	2009

23685 7590 05/19/2003

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EXAMINER
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CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

**09/890,377**

Applicant(s)

**Olek**

Examiner

**Arun Chakrabarti**

Art Unit

**1634**

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Mar 26, 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on Mar 26, 2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_

4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See attached sheet

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: \_\_\_\_\_

Claim(s) withdrawn from consideration: \_\_\_\_\_

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_

10. ☐ Other: \_\_\_\_\_

The request for reconsideration, filed on March 26, 2003, has been considered but does not place the application in condition for allowance because of the following reasons:

A) Applicant argues (page 3, last paragraph to page 4, line 9) that Herman et al reference teaches only the amplification of methylated fragments and does not teach the amplification of both methylated and unmethylated fragments of the instant invention. This argument is not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the amplification of both methylated and unmethylated fragments) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Moreover, Herman reference clearly teaches the amplification of both methylated and unmethylated fragments (Column 23, line 67 to Column 24, line 3).

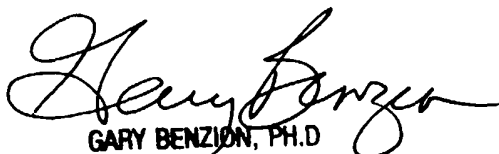
B) Applicant also argues (Page 4, last two sentences) that Herman reference does not teach the step(c) of removing any non hybridized probes from the immobilized DNA samples and there would be no reason to hybridize any probes to the MSP amplicates for the purpose of indicating methylation and there would be no reason to remove any non-hybridized probes. This argument is not persuasive. Herman clearly and inherently teaches the separation of non-hybridized probes in the Southern blot technique (Example 2 and Figure 1). Moreover, it is well known to an ordinary practitioner skilled in the art that in any hybridization reaction (no matter how specific the target sample is), there is always a molar excess of unhybridized probes, which must be removed by washing and other means to reduce the background signal of hybridization.

C) Applicant also argues (Page 5, first two lines and page 6, line 3 of third paragraph, and

page 8, line 3) that each references individually does not teach all the elements of the claimed invention. This argument is not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

D) Applicant also argues (Page 5, lines 3-4 and page 6, lines 5-9 of third paragraph, and page 8, lines 4-8) that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Koster since Koster states, "In addition, because the instant disclosed processes allow the nucleic acid fragments to be identified and detected at the same time by their specific molecular weights (an unambiguous physical standard), the disclosed processes are also much more accurate and reliable than currently available procedure (Column 4, lines 50-55)". Similar logic is applicable to other combinatory references.

In view of the response to arguments, the request for reconsideration has not been found persuasive and therefore not entered.

  
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